PEDIATRICS

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FAX TRANSMISSION: PAGES 8

TO: Mark Geier, MD

FAX #: 301.989.1543

FROM: Jerold F. Lucey, MD

DATE: January 27, 2004

RE: Verstraeten Article

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January 27, 2004

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Thomas Verstraeten MD
GlaxoSmithKline Biologicals
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1330 Rixensart, Belgium

Dear Dr. Verstraeten:

The journal is in a transition phase from publishing letters in print to publishing all letters electronically in our P3R section. In the future we plan to limit the length of all letters to 400 words.

We have received the following letter from Dr. Mark Geier, which will be published on our electronic pages section via P3R. We had originally planned on publishing your letter in print.

I now believe it would be best to publish your letter (# 2004-0004) to follow Dr. Geier's letter in P3R. You may want to revise and resubmit your letter via P3R.

This will result in more rapid publication probably within the next week.

I should point out that *Pediatrics* "did not violate" its disclosure rules regarding conflict of interest (see attached letter from Dr. DeStefano, which will be published as an erratum). All authors signed our standard conflict of interest statement. I will ask Dr. Geier to remove this statement about "violation" by *Pediatrics* from his letter.

Sincerely,

Jerold Lucey

Jerold F. Lucey, MD
Editor-in-Chief, *Pediatrics*

Attachments: Letter from Frank DeStefano, MD
P3R letter from Mark Geier, MD

Lucey, Jerold F

From: Horbar [horbar@VTOXFORD.org]
Sent: Tuesday, January 27, 2004 10:28 AM
To: Lucey, Jerold F
Subject: P3R

P3R view

Article citation:

ARTICLE:
Thomas Verstraeten, Robert L. Davis, Frank DeStefano, Tracy A. Lieu, Philip H. Rhodes, Steven B. Black, Henry Shinefield, Robert T. Chen, and for the Vaccine Safety Datalink Team
Safety of Thimerosal-Containing Vaccines: A Two-Phased Study of Computerized Health Maintenance Organization Databases
Pediatrics 2003; 112: 1039-1048 [Abstract] [Full text]

P3R ID: pediatrics_el;665

Article ID: 112/5/1039
Article Date: 1 November 2003

Study misses association between thimerasol and autism

27 January 2004

Mark R. Geier, geneticist and vaccinologist
The Genetic Centers of America,
David A. Geier

Send letter to journal:
Re: Study misses association between thimerasol and autism

Email Mark R. Geier, et al.

Letter to the Editor: The recent article, "Safety of Thimerosal-Containing Vaccines: A Two- Phased Study of Computerized Health Maintenance Organization Databases," by Verstraeteten et al. [1], which failed to find a consistent association between thimerosal in childhood vaccines and neurodevelopmental disorders, has a number of issues that need to be further addressed. First, the article failed to disclose that the head author, Dr. Thomas Verstraeten, has for the past several years work for GlaxoSmithKline, a vaccine manufacturer of thimerosal-containing vaccines. In addition, Nancy Pekarek, a company spokeswoman for GlaxoSmithKline, has written that Verstraeten since leaving the Centers for Disease Control and Prevention (CDC) has worked as an adviser as the study was finalized and prepared for publication. Presently, GlaxoSmithKline, potentially, faces a large number of lawsuits on the very issue that the paper discusses. The failure to disclose this conflict of interest on the part of Verstraeten is a clear violation of the disclosure rules published by Pediatrics, which state, "Conflict of interest for a given manuscript exists when a participant in the peer-review or publication process -- an author, reviewer or editor -- has ties to activities that could inappropriately influence his or her judgment, whether or not judgment is in fact affected. Financial relationships with industry (e.g., through employment, consultancies, stock ownership, honoraria, expert testimony...are usually considered to be the most important conflicts of interest... Public trust in the peer-review process and the credibility of published articles depend in part on how well conflict of interest is handled

during writing, peer review and editorial decision-making...Financial relationships and their effects are less easily detected than other conflicts of interest. Participants in peer review and publication should disclose their conflicting interests, and the information should be made available so that others can judge their effects for themselves." Second, this very study was the topic of secrete-closed meetings between members of the CDC and other government organizations, as well as members of the vaccine manufacturers held at Simpsonwood, Georgia from 7-8 June 2000. The transcript of this meeting has been obtained under the Freedom of Information Act. This transcript reveals that the study initially found statistically significant dose-response effects between increasing doses of mercury from thimerosal-containing childhood vaccines and various types of neurodevelopmental disorders. The transcript documents that the data was real and statistically significant for many types of neurodevelopmental disorders, but that the meeting participants expressed that the data had to be "handled." Despite, discussion about how to "handle" the data, some participants expressed concern that the work that had already been done, and would be obtained by others through the Freedom of Information Act. In this event, even if professional bodies expressed the opinion that there was no association between thimerosal and neurodevelopmental disorders, it was already too late to do anything. In addition, other participants expressed that the vaccine manufacturers were in a horrible position to be able to defend any lawsuits alleging a relationship between thimerosal and neurodevelopmental disorders, since no one would say with the available data that there was no relationship between thimerosal and neurodevelopmental disorders. Even Verstraeten, in an email following the Simpsonwood meeting, expressed surprise that the data was to be manipulated, stating that ones desire to disprove an unpleasant theory should not interfere with sound scientific methods to evaluate the relationship between thimerosal and neurodevelopmental disorders. Third, there are also significant issues about the methods used to determine the mercury dose that children receiving from thimerosal- containing vaccines. The authors in Table 1 of their manuscript, completely fail to mention that there were large numbers of thimerosal- free Diphtheria-Tetanus-acellular-Pertussis (DTaP) vaccines administered to children in the Health Management Organization (HMO)s analyzed. Thimerosal-free DTaP vaccine has been produced by GlaxoSmithKline since 1997. We have personally analyzed the Vaccine Safety Datalink (VSD) database determining that approximately one-third of the children receiving DTaP in the VSD from 1997 through 2000 were immunized with this vaccine, and that the children received thimerosal-free DTaP vaccines in various combinations, with some receiving four doses of thimerosal-free DTaP, some receiving three doses of thimerosal free DTaP and one dose of thimerosal-containing DTaP, some receiving two doses with and two doses without thimerosal, some receiving three with and one without thimerosal, and some receiving all four doses of thimerosal-containing DTaP. In order to evaluate whether Verstraeteten et al., did or did not take this into account, we analyzed Table 1 from their study for cumulative mercury exposures at the various ages of immunization. At one month, the possible mercury exposure was 12.5 micrograms of mercury according to the authors, which is appropriate because there was no potential thimerosal-free DTaP vaccine to take into account. At 2-3 months, the possible cumulative mercury exposure was 37.5-75 micrograms of mercury according to the authors. These potential possible cumulative mercury exposures could be generated by DTP and Hib vaccine separated or combined, or by thimerosal- free DTaP vaccine and Hib (i.e. both DTPH or thimerosal-free DTaP vaccine and Hib vaccine,

resulted in children being exposed to 25 micrograms of mercury). At 5-6 months, the possible cumulative mercury exposure was 75 or 125 micrograms according to the authors. The fact that the authors only list these two potential possible cumulative mercury exposure doses show that the authors failed to take into account the thimerosal-free DTaP vaccine made by GlaxoSmithKline, since children receiving one thimerosal- containing DTaP followed by one thimerosal-free DTaP vaccine, in addition to their two doses of hepatitis B vaccine and two doses of Hib vaccine received 100 micrograms of mercury, a mercury dose not mentioned in the table. At 6-7 months, the possible cumulative mercury exposure was 112.5 micrograms of mercury or 187.5 micrograms of mercury according to the authors. These potential possible cumulative mercury exposures show overwhelmingly that there is a significant error in the study. The intermediate mercury values children were exposed to also included: two thimerosal-containing and one thimerosal-free DTaP vaccine, with three doses of hepatitis B vaccine and three doses of Hib vaccine, for a total of 162.5 micrograms of mercury; and two thimerosal-free DTaP and one thimerosal-containing DTaP vaccine, with three doses of hepatitis B vaccine and three doses of Hib vaccine, for a total of 137.5 micrograms of mercury. These calculations indicate that Verstraeteten et al. did not take thimerosal-free DTaP vaccine into account in their study, or if they did, then their paper, as it stands, is replete with inaccurate information. Additionally, the fact that the VSD data contained large numbers of children who took thimerosal-free DTaP vaccine and large numbers of children who took thimerosal-containing DTaP vaccine allows a much more direct and powerful way to do the study by comparing these two groups, since this type of analysis would allow for overall evaluation of the effects of increasing doses of mercury from thimerosal in comparison to considerably lesser doses of mercury from thimerosal. We have done just such a study in VSD and have found that there were statistically significantly increased ($p < 0.0001$) relative risks of autism (relative risk = 27.6), mental retardation (relative risk = 5.7), and speech disorders (relative risk = 6.34) in a cohort receiving additional doses of mercury from thimerosal-containing DTaP vaccines in comparison to the cohort receiving thimerosal-free DTaP vaccines. We also found that among children taking a mixture of the thimerosal-containing and the thimerosal- free DTaP vaccines, there were increasing-dose response relationships between increasing doses of mercury from thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines for autism, mental retardation, and speech disorders. This finding has confirmed our previous epidemiologically studies examining the Vaccine Adverse Event Reporting System (VAERS) among children receiving thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines, and our analyses of the US Department of Education [2-4]. It also fits in with the observation that children with autism fail to excrete mercury in their hair and show large increases in the amount of mercury in their urine following chelation therapy in comparison to controls [5,6]. This finding is particularly troubling in light of the fact that Slikker [7] from the Food and Drug Administration has published that thimerosal crosses the blood-brain and placental barriers and results in appreciable mercury content in tissues including the brain, and because it has been shown by Baskin et al. [8] that micromolar concentrations of thimerosal are capable of causing significant damage to neurons. It also is in keeping with the many hundreds of peer-reviewed articles published over many decades and from many fields of medicine and science reporting on the harmful effects of thimerosal in humans, animals, isolated neurons, and other systems. Fourth, there is also a significant issue regarding the inclusion of children who received whole-cell

Diphtheria-Tetanus-Pertussis (DTP) vaccine and DTaP vaccine. The Institute of Medicine of the United States' National Academy of Sciences has determined that the evidence is consistent with a causal relationship between whole-cell DTP vaccine and permanent brain damage [9, 10]. In addition, despite the claim by Verstraeteten et al. that encephalopathies following whole-cell DTP occur only rarely, and therefore, this would be unlikely to have influenced the results of the study, some authors, such as Strom [11] reported that 1 in 6,000 children developed a neurological reaction and 1 in 17,000 children died or were left with a permanent neurological defect and Pollock and Morris [12] who reported that 1 in 8,500 children died or had a neurological disorder following whole-cell pertussis vaccination. Therefore, it is clear that the assumption by Verstraeteten et al. that the inclusion of whole-cell DTP vaccine would have limited effects upon the results of their study seems incorrect, but rather points to a serious confounder present in their study that makes evaluation of the effect of thimerosal more difficult to discern. In conclusion, because of a number of very serious issues have been raised and the critical importance of the issue, whether thimerosal causes neurodevelopmental disorders, we respectfully request that Verstraeten et al. consider withdrawing this study. In order to restore the badly damaged confidence in our much needed vaccine program, it is necessity that past errors be admitted, and that open investigations be conducted on vaccines issues. It is also essential that future vaccine decisions are made by physicians and scientists without even the appearance of conflicts of interest.

Dr. Mark R. Geier has been a consultant and expert witness in cases involving vaccine adverse reactions before the National Vaccine Injury Compensation Program and in civil litigation.

David A. Geier has been a consultant in cases involving vaccine adverse reactions before the National Vaccine Injury Compensation Program and in civil litigation.

References 1. Verstraeten T, Davis RL, DeStefano F, et al. Safety of thimerosal- containing vaccines: A two-phased study of computerized health maintenance organization databases. Pediatrics. 2003;112:1039-1048. 2. Geier MR, Geier DA. Neurodevelopmental disorders following thimerosal-containing vaccines: a brief communication. Exp Biol Med. 2003;228:660-4. 3. Geier MR, Geier DA. Thimerosal in childhood vaccines, neurodevelopment disorders, and heart disease in the United States. J Am Phys Surg. 2003;8 (1):6-11. 4. Geier DA, Geier MR. An assessment of the impact of thimerosal on childhood neurodevelopmental disorders. Pediatr Rehabil. 2003;6:97-102. 5. Bradstreet J, Geier DA, Kartzinel JJ, Adams JB, Geier MR. A case- control study of mercury burden in children with autistic spectrum disorders. J Am Phys Surg. 2003;8:76-79. 6. Holmes AS, Blaxill MF, Haley BE. Reduced levels of mercury in first baby haircuts of autistic children. Int J Toxic. 2003;22:277-285. 7. Slikker W. Developmental neurotoxicology of therapeutics: survey of novel recent findings. Neurotoxicology. 2000;21:250. 8. Baskin DS, Ngo H, Didenko VV. Thimerosal induces DNA breaks, caspase-3 activation, membrane damage, and cell death in cultured human neurons and fibroblasts. Toxicol Sci. 2003;74:361-368. 9. Howson CP, Howe CJ, Finebery HV, eds. Adverse Effects of Pertussis and Rubella Vaccines. Institute of Medicine. Washington, DC: National Academy Press; 1991. 10. Stratton KR, Howe CJ, Johnston RB, eds. DPT Vaccine and Chronic Nervous System Dysfunction: A New Analysis. Institute of Medicine. Washington, DC: National Academy Press; 1994. 11. Strom J. Is universal pertussis vaccination always

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
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November 26, 2003

DEC - 4 2003

Ralph D. Feigin, MD, Associate Editor
Pediatrics Editorial Office
Texas Children's Hospital
6621 Fannin St. (MC 1-3000)
Houston, TX 77030-2399

RE: Manuscript #2003/36/F The Safety of Thimerosal-Containing Vaccines: A Two-Phased Study of Computerized HMO Databases. Pediatrics 2003;112:1039-1048.

Dear Dr. Feigin:

We wish to request that an *erratum* be published regarding the above referenced manuscript. On page1039, toward the end of the first paragraph of the text, it states "...may have exceeded the 1994 EPA guidelines for exposure to organic Hg (1 ug/kg/d vs 3 ug/kg/day...." We neglected a decimal point and this should be corrected to read, "...may have exceeded the 1994 EPA guidelines for exposure to organic Hg (0.1 ug/kg/d vs 0.3 ug/kg/d ...." Given that questions have been raised about the manuscript not identifying the current employer of the first author, we would also like to include the following statement as part of the *erratum*: "For the record, Dr. Verstraeten is currently employed by GlaxoSmithKline, although as indicated in the published article when he worked on the study he was an employee of the Centers for Disease Control and Prevention."

Sincerely yours,

Frank DeStefano, M.D., MPH

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justified? Br Med J. 1960;2:1184-1186. 12. Pollock TM, Morris J. A 7-year survey of disorders attributed to vaccination in North West Thames region. Lancet. 1983;1:753-757.

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